

Claims

1. A purified polypeptide comprising an antibody, or a functional fragment thereof, that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, wherein said antibody
5 specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), or COLO-678 (DSMZ Accession No. 194) cells and not to non-neoplastic cells.
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2. The purified polypeptide of claim 1, wherein said neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell.
- 15 3. A purified polypeptide comprising an antibody, or a functional fragment thereof, that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, wherein said antibody specifically binds to a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell and not to a non-
20 neoplastic cell.

4. A purified polypeptide comprising an antibody, or a functional fragment thereof, that inhibits cell proliferation when bound to a neoplastic cell, but does not inhibit cell proliferation of a non-neoplastic cell, wherein said antibody specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), or COLO-678 (DSMZ Accession No. 194) cells and not to non-neoplastic cells.

10 5. The purified polypeptide of claim 4, wherein said neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell.

15 6. A purified polypeptide comprising an antibody, or a functional fragment thereof, that inhibits cell proliferation when bound to a neoplastic cell, but does not inhibit cell proliferation of a non-neoplastic cell, wherein said antibody specifically binds to a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell and not to a non-neoplastic cell.

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7. The purified polypeptide of claim 1, 3, 4, or 6, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:1.

25 8. The purified polypeptide of claim 1, 3, 4, or 6, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:3.

9. A purified polypeptide comprising an antibody, or functional fragment thereof, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:1.
- 5 10. A purified polypeptide comprising an antibody, or functional fragment thereof, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO:3.
- 10 11. A purified polypeptide comprising an antibody, or functional fragment thereof, wherein said polypeptide comprises the amino acid sequence of SEQ ID NOS:1 and 3.
- 15 12. The purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein said antibody is a human antibody.
13. The purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein said antibody is a monoclonal antibody.
- 20 14. The purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein said polypeptide is a functional fragment selected from the group consisting of V_L , V_H , F_V , F_C , Fab, Fab', and $F(ab')_2$.
- 25 15. The purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein said polypeptide is a functional fragment comprising a fragment that is substantially identical to the sequence of SEQ ID NO:1 or SEQ ID NO:3.

16. The purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein said polypeptide is a functional fragment comprising a fragment of the sequence of SEQ ID NO:1 or SEQ ID NO:3.

5 17. A cell that produces a polypeptide that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, wherein said polypeptide specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169),
10 COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), or COLO-678 (DSMZ Accession No. 194) cells and not to non-neoplastic cells.

15 18. The cell of claim 17, wherein said neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell.

20 19. A cell that produces a polypeptide that inhibits cell proliferation in a neoplastic cell to which it binds, but not in a non-neoplastic cell, wherein said polypeptide specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), or COLO-678 (DSMZ Accession No. 194) cells and not to non-neoplastic cells.

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20. The cell of claim 19, wherein said neoplastic cell is a colorectal adenocarcinoma, ovarian cancer, squamous cell lung carcinoma, or lobular mammary carcinoma cell.

21. A cell that produces a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:1.

22. The cell of claim 21, wherein said polypeptide comprises the
5 sequence of SEQ ID NO:1.

23. A cell that produces a polypeptide that comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:3.

10 24. The cell of claim 23, wherein said polypeptide comprises the sequence of SEQ ID NO:3.

25. A cell that produces a polypeptide that comprises the amino acid sequence of SEQ ID NOS:1 and 3.

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26. The cell of claim 17, 19, 21, 23, or 25, wherein said cell is a hybridoma.

27. A method of generating the cell of claim 17, said method
20 comprising the steps of:

(a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

(b) determining whether said hybridoma produces a polypeptide that
25 induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, and

(c) determining whether said hybridoma produces polypeptide that specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), or COLO-678 (DSMZ Accession No. 194) cells and not to non-neoplastic cells.

28. A method of generating the cell of claim 19, said method comprising the steps of:

10 (a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

(b) determining whether said hybridoma produces a polypeptide that inhibits proliferation in a neoplastic cell to which it binds, but does not inhibit proliferation in a non-neoplastic cell, and

15 (c) determining whether said hybridoma produces polypeptide that specifically binds to at least one of HT-29 (ATCC Accession No. HTB-38; DSMZ Accession No. ACC 299), CACO-2 (ATCC Accession No. HBT-37; DSMZ Accession No. ACC 169), COLO-320 (DSMZ Accession No. ACC 144), COLO-206F (DSMZ Accession No. ACC 21), or COLO-678 (DSMZ Accession No. 194) cells and not to non-neoplastic cells.

29. Use of the purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11 in a method of diagnosing a neoplasm in a mammal, said method comprising the steps of:

25 (a) contacting a cell or tissue sample of said mammal with the purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, and

(b) detecting whether said purified polypeptide binds to said cell or tissue sample, wherein binding of said purified polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm.

5 30. The use of claim 29, wherein said mammal is a human.

31. The use of claim 29, wherein said neoplasm is a colorectal adenocarcinoma, an ovarian cancer, a squamous cell lung carcinoma, or a lobular mammary carcinoma.

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32. The use of claim 29, wherein said polypeptide is an antibody.

33. The use of claim 29, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a
15 fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

34. The use of claim 29, wherein said polypeptide is conjugated to a protein purification tag.

20 35. The use of claim 34, wherein said protein purification tag is cleavable.

36. Use of the purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11 in a method of treating a proliferative disorder in a mammal, said method
25 comprising the step of contacting a cell or tissue sample with the purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein binding of said purified polypeptide to said cell or tissue sample results in the induction of apoptosis of said cell or tissue sample.

37. The use of claim 36, wherein said mammal is a human.

38. The use of claim 36, wherein said proliferative disorder is a colorectal adenocarcinoma, an ovarian cancer, a squamous cell lung carcinoma,
5 or a lobular mammary carcinoma.

39. The use of claim 36, wherein said polypeptide is an antibody.

40. The use of claim 36, wherein said polypeptide is conjugated to a
10 detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

41. The use of claim 40, wherein said detectable agent is capable of inducing apoptosis of said cell or tissue sample.

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42. The use of claim 36, wherein said polypeptide is conjugated to a protein purification tag.

43. The use of claim 42, wherein said protein purification tag is
20 cleavable.

44. Use of the purified polypeptide of claim 1, 3, 4, 6, 9, 10, or 11 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell or tissue sample with the purified
25 polypeptide of claim 1, 3, 4, 6, 9, 10, or 11, wherein binding of said purified polypeptide to said cell or tissue sample results in a reduction in proliferation of said cell or of a cell in said tissue sample.

45. The use of claim 44, wherein said mammal is a human.

46. The use of claim 44, wherein said proliferative disorder is a colorectal adenocarcinoma, an ovarian cancer, a squamous cell lung carcinoma,
5 or a lobular mammary carcinoma.

47. The use of claim 44, wherein said polypeptide is an antibody.

48. The use of claim 44, wherein said polypeptide is conjugated to a
10 detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

49. The use of claim 48, wherein said detectable agent is capable of inhibiting cell proliferation of said cell or tissue sample.

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50. The use of claim 44, wherein said polypeptide is conjugated to a protein purification tag.

51. The use of claim 50, wherein said protein purification tag is
20 cleavable.

52. A medicament comprising the purified polypeptide of any one of claims 1, 3, 4, 6, 9, 10, or 11 in a pharmaceutically acceptable carrier.

25 53. A diagnostic agent comprising the purified polypeptide of any one of claims 1, 3, 4, 6, 9, 10, or 11.